MEDICINAL GAS
FREQUENTLY ASKED QUESTION (FAQ)

GENERAL

	QUESTION	ANSWER
1.	What is the scope covered under the regulation for medicinal gases?	The scope covers medicinal gas classified as a medicinal product/drug and in cylinders intended for inhalation, which are manufactured in a filling plant from bulk liquid gas: a) **Oxygen, O_2** (not less than 99 %v/v oxygen) b) **Carbon dioxide, CO_2** (not less than 99%v/v carbon dioxide) c) **Nitrous oxide, N_2O** (not less than 98%v/v nitrous oxide) d) ***Nitric oxide, NO** (not less than 99%v/v nitric oxide) e) **Nitrous oxide/Oxygen mixture** (50%:50%) f) **Medical air** (oxygen/nitrogen mixture, 19.5–23.5% v/v of oxygen (O_2)) *Nitric oxide, NO (Group B Scheduled Poison)
2.	What type of gases are not within the scope of regulation for medicinal gases?	Gases that are not within the scope of regulation for medicinal gases are as follow: a) Industrial gases b) Recreational gases (e.g. oxygen gas for diving, mountain climbing) c) Gases for animal use (veterinary) d) Gases for cosmetic/aesthetic purpose e) Gases for laboratory use (e.g. gas for freezing of tissue samples, calibration gas) f) Gases that are manufactured, mixed and handled (including extemporaneous preparation) in hospitals for patients own use. g) Gases classified as medical devices which will be regulated by the Medical Device Authority (MDA) h) Gases or gas mixtures whose mode of action is achieved primarily by physical in nature and not achieved primarily based on pharmacological, immunological or metabolic action in/on the body, such as gases for insufflation of the abdominal cavity for laparoscopy and gases for removal of warts (e.g., liquid nitrogen).
3.	Is the portable medical oxygen intended for ambulatory patients use covered under the regulation for medicinal gases?	Yes. Portable medical oxygen intended for the administration to patients for medicinal purpose such as anaesthetic, therapeutic, prophylactic and diagnostic use are regulated by Drug Control Authority (DCA).

4.	Can a registered medicinal gas be sold for purposes other than medical usage?	No. A registered medicinal gas product is to be used for medicinal purpose only.
5.	What are the directives/ guidelines issued by NPRA relating to medicinal gases?	These are the guidance documents which are available from NPRA website. 1. Direktif Berkenaan Pengukuhan Pelaksanaan Kawalan Regulatori Ke Atas Produk - Produk Gas Perubatan Dan Penggunaan Guideline On Registration Of Medicinal Gases 2. Guidance Note: Good Manufacturing Practice (GMP) Inspection On Medicinal Gases Manufacturers In Malaysia 3. Drug Registration Guidance Document (DRGD)
6.	Is Good Distribution Practice (GDP) required for the regulation of medicinal gas products?	Yes. • Manufacturers are required to comply with the principles of Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP). • Importers and Wholesalers are required to comply with the principles of Good Distribution Practice (GDP). • For GDP guideline, please refer to the Guideline on Good Distribution Practice (Third Edition, 2018).
7.	Is liquid medical oxygen supplied via vacuum insulated evaporator (VIE) tank installed at the healthcare facilities and oxygen generated on site (healthcare facility) included in this scope?	No. Please refer to Medical Device Authority (MDA) for the regulation and requirements on the devices/system used for the gas supply.

REGISTRATION

	QUESTION	**ANSWER**
8.	What is the implementation date for registration of medicinal gas products?	The implementation date has been divided in phases starting with the voluntary submission for medicinal gas products (medicinal gas in cylinder) from 1st January 2022. The registration will be made mandatory from 1st January 2023 onwards.
9.	Who is required to register for the medicinal gas products?	The application shall be submitted by a locally incorporated company who has a registered business entity with the Suruhanjaya Syarikat Malaysia (SSM). The applicant, also known as the Product Registration Holder (PRH) should be responsible for quality, safety and efficacy information that is submitted to NPRA in support of the product registration application.

10.	What is the specific requirement for product name?	Product name shall consist of dosage form and strength (for single active ingredient product) e.g. X Brand Oxygen Medicinal Gas 100%v/v Product name is defined as a name given to a product, which may either be a proprietary name (an invented name); or a generic name (common name) or scientific name, together with a trade mark or the name of the manufacturer.
11.	Is liquid oxygen used for medicinal purpose required to be registered?	Only finished products (medicinal oxygen gas **in cylinder**) are required to be registered with the Drug Control Authority (DCA).
12.	Are gas cylinders required to be registered?	The empty gas cylinder is regulated by Medical Device Authority (MDA). Therefore, gas cylinders should comply with medical device requirements. A proof of submission for endorsement letter **to** MDA or endorsement letter **from** MDA for the cylinder shall be submitted to NPRA during medicinal gas product registration application. Gas cylinder: a) Gas Cylinder (empty) b) Gas Cylinder (empty) with valve c) Gas Cylinder (empty) with integrated pressure regulator
13.	Does the same medicinal gas product that has different functions required to be registered with both NPRA and MDA?	If the medicinal gas in a cylinder (containing same strength of gas) that has dual functions as both medicinal product/drug and medical device, the product is required to be registered with the Drug Control Authority (DCA) only. Therefore, the registration submission for the medicinal gas should be submitted to NPRA. The cylinder component however should comply with the medical device requirements.
14.	What are the references used for the specification of medicinal gases?	Pharmacopoeia such as USP, BP and Ph.Eur will be used as reference for the specification of the medicinal gases.
15.	Can we state the required information for labelling requirement in separate label on one cylinder?	All information required for labelling requirement must be stated in one/single label. Any others/extra information required by other regulation (e.g. OSHA) to be stated on the label is subject to further evaluation. NPRA may consider second label contain the information such as Batch Number, Manufacturing Date and Expiry Date.

16.	Imported medicinal gas product (medicinal gas in cylinder) is included in the scope. Can we register an imported product that has not been marketed in the exporting country?	For the purpose of registration, the medicinal gas product have to be marketed in the exporting country. Therefore, a Certificate of Pharmaceutical Product (CPP) or Certificate of Free Sale (CFS) should be submitted during registration submission as a market evidence.
17.	Medicinal gas product is classified as pharmaceutical product. Are the registration fee and evaluation time line same as other pharmaceutical products?	**Yes.** Both registration fee and evaluation timeline are as stated in the Drug Registration Guidance Document (DRGD) for pharmaceutical product.
18.	What is the time frame for manufacturers to ensure the approved labels are used on ALL cylinders filled by them?	The implementation of cylinder labelling requirements for registered medical gas products is within six (6) months from the registration date. Changes can be implemented immediately after submission or within 6 months.
19.	As stated in DRGD, Second Source is defined as a product that is the same as the product from the first source in all aspects, except for the site of manufacture. Can medicinal gas product (e.g: Oxygen gas in cylinder) manufactured by more than one manufacturer?	The existing products (products in the market before 1st January 2023) will be allowed to be manufactured in more than one facility provided all facilities had been inspected and complied with good manufacturing practice (GMP) requirements. Such permission however is limited to product that is similar in all aspects (e.g. specifications, manufacturing process, etc.), except being manufactured in different site. New product registration applications receive after 1st January 2023 will only be allowed with two manufacturing sites.
20.	How to make amendment for registered medicinal gas product?	Throughout the life cycle of a registered product, changes to improve product efficacy, quality and safety are likely to occur. Therefore, the applicant shall inform NPRA of any changes or amendments made to particulars of a registered product through variation application (online).
21.	Who is qualified to release a passed medicinal gas batch? Must a pharmacist involved?	Please refer to definition of authorized person. Registered Pharmacist with *type A licence is required if the medicinal gas product containing active ingredient listed in poison list (scheduled poison). *Type A Licence: issued to a pharmacist to import, store and deal generally all poisons by wholesale and retail or by wholesale only or by retail only.

22.	Should a sample submit for registration purpose?	Submission of sample prior registration is not required. However, the PRH is responsible to provide samples if requested by the Authority.
23.	Do we need to submit Certificate of Analysis (CoA) for each pack size?	CoA for each pack size is required if the packaging materials are different.

GOOD MANUFACTURING PRACTICE (GMP)

	QUESTION	**ANSWER**
24.	What are the GMP requirements for medicinal gas manufacturers?	Manufacturers are required to comply to PIC/S Guide to Good Manufacturing Practice for Medicinal Products and related Annexes.
25.	What are the GMP requirements for the active pharmaceutical (API) medicinal gas manufacturer?	GMP certificate/GMP Inspection reports/Declaration on Quality Management System (QMS) is required as a GMP compliant evidence. The acceptable GMP compliance evidence for API manufacturer are listed as follows: A) GMP Certificate or GMP Inspection Report issued by: i. Pharmaceutical Inspection Co-Operation Scheme (PIC/S) Participating Authorities; ii. World Health Organization (WHO) or; iii. Drug Regulatory Authority B) Declaration on Quality Management System for Medicinal Gas Active Pharmaceutical Ingredient (API) Manufacturer by Competent Person (refer to GUIDELINE ON REGISTRATION OF MEDICINAL GASES).
26.	How to apply for GMP Inspection?	The stepwise GMP inspection process is well explained in the **Guidance Note: GMP Inspection on Medicinal Gases Manufacturers in Malaysia, 1st Edition August 2021.** The GMP elements to be inspected are mentioned in the same guidance document. For other GMP inspection related questions, please refer to FREQUENTLY ASKED QUESTIONS (FAQs) ABOUT GMP INSPECTION
27.	What is the definition & qualification required to be the authorised/competent person?	An **authorised person** is referring to a Competent Person in Quality Control Department which has been appropriately trained and qualified, appointed by Senior Management to release the medicinal gas product for distribution in the market. The appointed personnel should have such duties recorded in written job descriptions and adequate authority to carry out their responsibilities.

		A **competent person** is a trained, qualified and experienced Quality Control Department personnel that has been appointed by Senior Management. This has been highlighted in CDCR 1984, Regulation 19. Personnel whereby a licensed manufacturer shall ensure that all personnel employed at all levels of manufacture- (a) possess suitable qualifications required for their jobs; (b) have adequate experience and are technically competent; (c) are regularly trained during their employment for the purposes of keeping up to date with any advances or changes; and (d) are medically examined regularly. Appointed personnel should have such duties recorded in written job descriptions and adequate authority to carry out their responsibilities.

PHARMACOVIGILANCE

	QUESTION	**ANSWER**
28.	What is an Adverse Drug Reaction (ADR) and when it is reportable to NPRA?	The World Health Organization defines an ADR as "**any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for** prophylaxis, diagnosis, or therapy of disease, or for the modification of **physiological function**." With the use of medicinal gases, some common physiological side effects may include (but not limited to): blurred vision, confusion, dizziness, sweating or unusual tiredness or weakness. If any of these ADRs are suspected for a locally registered product, they should be reported to the NPRA.
29.	How to report an ADR to NPRA?	If you are representing a **company or product registration holder**, please download the CIOMS form (https://cioms.ch/cioms-i-form/), complete and submit to the Pharmacovigilance Section at: fv@npra.gov.my If you are a **healthcare professional**, please complete and submit the ADR webform at this link: https://www.npra.gov.my/index.php/en/health-professionals/reporting-adr.html If you are a **consumer**, please complete and submit the ADR webform at this link: https://www.npra.gov.my/index.php/en/consumers/reporting/reporting-side-effects-to-medicines-conserf-or-vaccines-aefi-2.html Each ADR report submitted should involve only **ONE (1)** patient with the minimum required information of an identifiable reporter, patient, ADR description and product.

30.	What is the guidance available for the Product Registration Holder (PRH) to report an ADR to NPRA?	The PRH should report any ADR that occurs in Malaysia according to the guidance including the timelines detailed in the Malaysia Guidelines on **Good Pharmacovigilance Practices (GVP) for Product Registration Holders, First edition, August 2021.** As medicinal gases are packaged in cylinders, you may also refer to the post-registration requirements detailed in the **Guideline For Registration Of Drug-Medical Device And Medical Device-Drug Combination Products, 5th edition, Jan 2023.**